REMARKS/ARGUMENTS

Claims 1-54 were pending in the present application. Claims 18-49 were withdrawn from consideration, and claims 1-17 were rejected. By this amendment, claims 1-17 have been amended, claims 18-49 are canceled without prejudice, and new claims 50-54 have been added. No new matter has been introduced. In particular, new claims 50-53 are supported by the specification at least on page 15, lines 10-19 and on page 20, Example 2. New claim 54 is supported by the specification at least on page 17, line 37.

Claim Objections

Claims 2, 3 and 6 were objected to for various informalities. Claims 2, 3 and 6 have been amended to correct the noted informalities. Applicants respectfully submit that the amendments obviate the grounds for the objection. Withdrawal of the objection to claims 2, 3 and 6 is respectfully requested.

Claim Rejections under 35 U.S.C. §112

Claims 1-17 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Specifically, the Examiner alleges that (a) there is insufficient antecedent basis for the limitation "the target sequence" in claim 1, (b) the phrase "suitable hybridization condition" in claim 1 is not defined the specification, (c) it is not clear what is meant by the term "probing" in claim 1, (d) SEQ ID NO:10 in claim 9 is not designed for targeting a tumor marker, (e) claim 13 uses improper Markush group language, and (f) claim 16 is drawn to a method for targeting a gene but not a mRNA.

Claims 1, 9, 13 and 16 have been amended to better describe the claimed invention. Applicants respectfully submit that the amendments obviate the grounds for the rejections. Withdrawal of the rejections to claims 1-17 under 35 U.S.C. §112, second paragraph, is respectfully requested.

Claim Rejections under 35 U.S.C. §102

Claims 1-5 stand rejected under 35 U.S.C. §102(a) as being anticipated by Span et al. (hereinafter "Span"), claims 1-3 and 14 stand rejected under 35 U.S.C. §102(a) as being anticipated by Vijayanathan et al. (hereinafter "Vijayanathan"), claims 1-4 and 16 stand rejected under 35 U.S.C. §102(a) as being anticipated by Singer et al. (hereinafter "Singer") as evidenced by Vogelstein et al. (hereinafter "Vogelstein"), claims 1-3 and 10 stand rejected under 35 U.S.C. §102(a) as being anticipated by Wen et al. (hereinafter "Wen"), claims 1-4, 7-10, 16 and 17 stand rejected under 35 U.S.C. §102(e) as being anticipated by US 20060127940 to Bao et al. (hereinafter "Bao 940"), claims 1-4, 6, 12 and 14 stand rejected under 35 U.S.C. §102(e) as being anticipated by Harbeck et al. (hereinafter "Harbeck"), and claims 1-4, 7-10, 16 and 17 stand rejected under 35 U.S.C. §102(e) as being anticipated by US 7,297,494 to Bao et al. (hereinafter "Bao 494"). Applicants respectfully traverse the rejections.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. Of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).*

Independent claim 1, as amended, is directed to a method of detecting the presence of tumor marker mRNA in a sample comprising: i) incubating a cell with one or more oligonucleotides that hybridize to the mRNA of one or more tumor markers, wherein each oligonucleotide comprises at least one linked energy donor moiety and at least one linked energy acceptor moiety, wherein said oligonucleotide forms a stem-loop hairpin and wherein said donor and acceptor moieties are separated by at least a portion of a nucleobase sequence that is complementary to a target sequence in said mRNA, and wherein each oligonucleotide hybridizes to the mRNA of a different tumor marker and emits a fluorescent signal after hybridization with the corresponding mRNA; ii) detecting fluorescent signals emitted by the one or more oligonucleotide; and iii) quantitating the presence of a tumor marker based upon the fluorescent signals detected in step (iii).

Claim 1 recites the use of molecular beacons to detect tumor marker mRNA in a cell by **directly** incubating the cell with the molecular beacons. In contrast, Span, Singer, Vogelstein, Wen and Harbeck describe methods of detection of tumor marker mRNA by RT-PCR. The RT-PCR procedure requires the extraction of mRNA from a cell and subsequent conversion of mRNA to cDNA and amplification of the cDNA. The molecular beacon is then used to hybridize to the amplified DNA products. Span, Singer, Vogelstein and Harbeck do not teach or suggest incubating a molecular beacon directly with a cell, as recited in claim 1.

Vijayanathan describes direct measurement of the association constant of Her2/neu antisense oligonucleotide to its target RNA sequence using a molecular beacon. The molecular beacon is incubated with synthetic RNA molecules, not intact cells. Therefore, Vijayanathan fails to teach or suggest incubating a molecular beacon directly with a cell, as recited in claim 1.

Bao 940 and Bao 494 describe the use of dual molecular beacons to detect the level of gene expression. For each biomarker gene, a pair of molecular beacons labeled with different fluorescence dyes and quenchers are used. In other words, the methods described in Bao 940 and Bao 494 require two molecular beacons for each biomarker. The instant claim 1, as amended, recites that "each oligonucleotide hybridizes to the mRNA of a different tumor marker." Therefore, Bao 940 and Bao 494 do not anticipate the claimed invention.

Accordingly, Applicants respectfully submit that claim 1 is patentable over the cited references because none of the cited references mentions every element recited in claim 1. Applicants further submit that claims 2-17 and 50-54 are patentable over the cited references because they depend from claim 1 and recite additional patentable subject matter.

In view of the foregoing, these grounds of rejection have been obviated and withdrawal of the rejection under 35 U.S.C. §102 to claims 1-17 is respectfully requested.

CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to contact Ping Wang, M.D. (Reg. No. 48,328) at 202-842-0217.

Respectfully submitted,

MORRIS, MANNING & MARTIN, LLP

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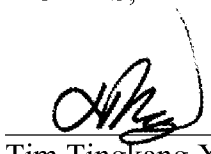

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